REMARKS

Claims 1-20 remain in this application. Claims 11 and 20 are currently amended. Support for the amendments can be found in the specification and original claims as file. No new matter has been added.

CLAIM REJECTIONS - 35 USC § 112

At page 3, the Office Action rejects claims 11, 12 and 20 under 35 U.S.C. § 112, second paragraph. Applicants respectfully traverse the rejection.

Currently amended claims 1 and 20 address the issue noted in the Office Action and further clarify the lysozyme component. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

It also appears that the Office Action recognizes that claims 11, 12 and 20 are free of the prior art and are directed to allowable subject matter.

CLAIM REJECTIONS - 35 USC § 103

At page 3, the Office Action rejects claims 1-10 and 13-19 under 35 U.S.C. § 103(a) as being unpatentable over SINGH et al. (US 2003/0185884) in view of FREY (US 2001/0043915), GB 941664 and HATSUYA et al. (US 5342840), and as evidenced by

"Resolution Oeno." Applicants respectfully traverse the rejection.

Claim 1 is directed to a pharmaceutical composition for the treatment of hypoptyalism, comprising pilocarpine combined with at least one bioadhesive polymer so as to allow dissolution and local attachment to the tissues of the buccopharyngeal cavity.

SINGH relates to a pilocarpine delivery composition used to raise the pH of the buccal cavity so that pilocarpine can be delivered in a lipophilic form capable of crossing the buccal membrane. The delivery composition raises the pH of the buccal cavity through a combination of buffer agents. The composition is particularly suited for a chewing gum (see, Abstract).

Importantly, SINGH designed a system to deliver pilocarpine in a lipophilic form. For example, SINGH states "For a substance to be absorbed through the mucosal membrane of the buccal cavity, it has to be presented in a lipophilic form." (See, paragraph [0034]). SINGH describes a buffer formulation that will "restore free form lipophilicity of pilocarpine and thereby facilitating in vivo absorption via increased permeability." (See, paragraph [0057]). The SINGH system is based on creating a pH environment that allows the drug to exist in "ready to be absorbed lipophilic form." (See, for example, paragraphs [0040] and {0064]).

In contrast to SINGH, the present composition does not produce a "lipophilic" pilocarpine. In fact, one of ordinary

skill in the art would recognize that pilocarpine is not lipophilic. For example, the Martindale Complete Drug Reference describes pilocarpine as "An alkaloid obtained from the leaves of jaborandi . . . soluble in water, in alcohol and in chloroform . . ." (See, Martindale included in Appendix). In fact, pilocarpine is amphiphilic and this allows dissolution both in water and in an organic solvent. Thus, SINGH incorrectly teaches that a pH buffer would turn an amphiphilic substance into a lipophilic one.

In contrast to SINGH, the present composition clearly defines the true nature of pilocarpine: amphiphilic and small molecular weight and freely soluble. Thus, pilocarpine can spontaneously cross buccal mucous membranes when in close contact with the membranes. Claim 1 features a composition of pilocarpine combined with at least one bioadhesive polymer so as to allow dissolution and local attachment to the tissues of the buccopharyngeal cavity. This allows the pilocarpine to cross the buccal mucous membrane.

Claim 9 is directed to a sublingual tablet for the treatment of hypoptyalism, comprising the pharmaceutical composition according to claim 1. SINGH fails to teach or suggest any specific sub-lingual form or application of pilocarpine that would bring local effectiveness to the mucous floor. SINGH describes a chewing gum based pilocarpine formulation as a systemic "oral route" of administration. Indeed, chewing a pilocarpine gum leads to a maximum salivary flow production thus diluting the active ingredient which is immediately swallowed.

One does not keep saliva volumes voluntarily retained in the mouth and swallowing is a typical automatic reflex from the non-cortical central nervous system. Thus, the SINGH composition is swallowed and metabolized similar to a pilocarpine pill or capsule.

In distinction, claim 9 features a tablet for sublingual application providing a slow and local coating/releasing galenic structure, allowing for a local mucous fixation/passage of the amphiphilic freely soluble drug. The sublingual form slowly releases pilocarpine under the tongue to be passively and slowly absorbed as it is coated by polymers onto the local mucous tissue area. In this way, the present composition induces a local per-mucous contact with the mucous membrane, stimulating the muscarinic receptors of the sero-mucous salivary micro-glands. SINGH fails to teach or suggest this type of sublingual application.

For at least these reasons, SINGH fails to teach or suggest the compositions of claims 1 and 9.

FREY relates to methods of delivering cytokines to the central nervous system and lymphatic system by way of a tissue innervated by the trigeminal nerve and/or olfactory nerve. First of all, one of ordinary skill would not modify the compositions of SINGH by anything disclosed in FREY.

FREY describes the administration of cytokines, i.e. peptide molecules, for the treatment of severe systemic and

neurobiologic or immune pathologies. In distinction, the presently claimed compositions are directed to hypoptyalism treatment using pilocarpine, an alkaloid extracted from *pilocarpus jaborandi*. One of ordinary skill would not connect such an alkaloid to the teachings related to cytokines.

Although the Office Action contends that it is well known to combine two or more ingredients each of which is taught by the prior art for the same purpose in order to form a third composition which is useful for the same purpose, this principle does not apply to the combination of SINGH and FREY. As detailed above, the compositions of SINGH and FREY are not for the same purpose. One of ordinary skill would not combine ingredients from FREY with those of SINGH, and such a third composition would not be useful for either of SINGH or FREY.

The present claims are directed to a composition designed for dissolution and local attachment to the tissues of the buccopharyngeal cavity. In distinction, FREY's routes of delivery are defined as tissues innervated by the trigeminal nerve, the olfactory nerve or a combination thereof. The cytokine is absorbed through the tissue and transported to the central nervous system of the mammal. One of ordinary skill would not utilize the teachings of FREY to produce a composition for the buccal application of pilocarpine.

HATSUYA relates to cycloprane derivatives having anti-viral activity. Various pharmaceutical compositions are contemplated including tablet form. HATSUYA, however, fails to

teach or suggest any composition of cycloprane combined with at least one bioadhesive polymer so as to allow dissolution and local attachment to the tissues of the buccopharyngeal cavity, as presently featured in present claim 1. HATSUYA also fails to teach or suggest a sublingual tablet formulation as featured in present claim 9. Furthermore, HATSUYA fails to remedy the deficiencies of SINGH and FREY detailed in the above remarks.

For all of these reasons, SINGH, FREY, GB 941664 and HATSUYA, alone or in any combination, fail to teach or suggest, and would not have rendered obvious, claims 1-10 and 13-19. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CONCLUSION

Entry of the above amendments is earnestly solicited. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following item(s):

☒ - MARTINDALE, The Complete Drug Reference, 32nd Edition.